

Table 5. Putatively Pathogenic Mutations

Exon	Accession Number	Nucleotide Change	Amino Acid Change	Protein Domain
11	ss49853007	1256C>T	p.A419V	
19	ss49853008	2264C>T	p.P755L	
19	ss48398570	2378G>T	p.R793M	
21		2789A>G	p.Q930R	
23		3200G>A	p.R1067Q	LRR
24		3287V>G	p.S1096C	LRR
24	ss48398571	3342A>G	p.L1114L	LRR
25	ss48398572	3364A>G	p.I1122V	LRR
25		3451G>A	p.A1151T	LRR
27		3683G>C	p.S1228T	LRR
29	rs17466213	4111A>G	p.I1371V	Roc
31	ss48398558	4322G>A	p.R1441H	Roc
32	ss48398559	4541G>A	p.R1514Q	COR
34	ss48398562	4937T>C	p.R1628P	COR
38		5605A>G	p.M1869V	COR
38	ss48398563	5606T>C	p.M1869T	COR
38		5620G>T	p.E1874STOP	COR
39		5822G>A	p.R1941H	MAPKKK
41	ss48398574	6035T>C	p.I2012T	MAPKKK
47		7067C>T	p.T2356I	WD40
48 ¹	ss48398568	7153G>A	p.G2385R	WD40

Putatively pathogenic variants are so-called because they have usually been observed only in small kindreds (obviating co-segregation studies with the phenotype) or found in a small number of simplex cases and appear to be absent in controls. Comprehensive frequency and case-control studies are necessary to clarify the effect of these variants on PD susceptibility and disease development [Paisan-Ruiz et al 2004; Zimprich et al 2004; Berg et al 2005; Farrer et al 2005; Khan et al 2005; Mata, Kachergus et al 2005; Skipper et al 2005; Zabetian et al 2005; Di Fonzo, Wu-Chou et al 2006; Schlitter et al 2006; Tomiyama et al 2006].

1. A postulated 'risk factor' [Tan et al 2006]

Table 6. Pathogenic Mutations

Exon	Accession Number	Nucleotide Change	Amino Acid Change	Protein Domain
31	ss48398556	4321C>T	R1441C	Roc
31	ss48398557	4321C>G	R1441G	Roc
35	ss48398573	5096A>G	Y1699C	COR
41	ss48398564	6055G>A	G2019S	MAPKKK
41	ss48398575	6059T>C	I2020T	MAPKKK

To fully elucidate the pathogenicity of *LRRK2* mutations, it will be necessary to demonstrate co-segregation of the mutation with the disease phenotype within large kindreds and absence of the mutation in large numbers of control individuals of the same ethnicity. The use of two or more case-control series of different ethnic backgrounds will resolve the potential of the variant as a 'risk factor' [Paisan-Ruiz et al 2004, Zimprich et al 2004, Di Fonzo et al 2005, Gilks et al 2005, Kachergus et al 2005, Nichols et al 2005]